Guidance for Industry

Notifying FDA of Fatalities Related to Blood Collection or Transfusion

DRAFT GUIDANCE

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Comments and suggestions regarding this draft document should be submitted by the date provided in the *Federal Register* notice announcing the availability of the draft guidance. Submit comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that published in the *Federal Register*.

Additional copies of this draft guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this draft guidance contact Lois Simmons at 301-827-6220.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
June 2002

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GUIDANCE FOR INDUSTRY

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This guidance represents the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. PURPOSE

This document's goal is to help you, a blood collection or transfusion facility, report fatalities related to blood and blood component (blood) collection or blood transfusion to us, FDA's Center for Biologics Evaluation and Research (CBER). The FDA uses mandatory language such as *shall, must* and *require* when referring to statutory or regulatory requirements. We use non-mandatory language such as *should, may, can,* and *recommend* when referring to guidance.

II. BACKGROUND

The good manufacturing practice regulations (GMPs) for blood and blood components, 21 CFR 606.170(b), require that you report fatalities related to blood collection or transfusion to CBER. Section 606.170(b) states:

> "When a complication of blood collection or transfusion is confirmed to be fatal, the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, shall be notified by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible; a written report of the investigation shall be submitted to the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, within 7 days after the fatality by the *collecting facility* [emphasis added] in the event of a donor reaction, or by the *facility that performed the compatibility tests* [emphasis added] in the event of a transfusion reaction."

III. HOW TO NOTIFY FDA

Section 606.170(b) states that you may report a fatality by telephone, facsimile, express mail, or electronically transmitted mail (e-mail). You should submit the initial notification by e-mail, if possible, and you will receive an e-mail confirmation receipt from us. If e-mail is not feasible, please notify us by telephone or facsimile. Facsimile notification will only be reviewed during

customary working hours or the next business day. You should submit 7-day follow up reports by e-mail, facsimile, or express mail.

- E-mail: fatalities2@cber.fda.gov
- Telephone/voice-mail number: 301-827-6220
- Fax number: 301-827-6748, Attn: CBER Fatality Program Manager
- Express mail address:
  Office of Compliance and Biologics Quality/CBER
  Attn: Fatality Program Manager (HFM-650)
  1401 Rockville Pike, Suite 200N
  Rockville, MD 20852-1448

IV. INITIAL NOTIFICATION

There is no required FDA form or format for notifying us of fatalities related to blood transfusion or blood collection. You should provide at least the following information so we can evaluate the potential public health significance of the event.

- Date and time of the notification.
- Your name, title, telephone number with area code and your fax number (if available).
- Your facility's name, mailing address, and FDA registration number (if applicable). **NOTE**: Transfusion services that do not routinely collect or process blood or blood components are not required to register with FDA and, therefore, do not usually have a registration number.
- Age and sex of the deceased.
- Date, time, and cause or suspected cause of death (briefly describe what happened).
- If an autopsy was or will be performed.
- Name and address of facility where the fatality occurred if different from your facility.
- Please also include in the initial notification the information listed in A, B, or C below, as appropriate:

A. Patient/Recipient Fatality

- Transfusion date(s),
- Blood/blood component(s) and unit number(s) of product(s) that may be implicated,
- Name and address of facility(ies) providing the blood,
- Brief description of events that led to the fatality – include underlying medical condition or disease and circumstances necessitating this hospitalization, reason for transfusion, how the patient initially responded to the transfusion, any medical intervention taken or response to the reaction, and time from initiating the transfusion to patient's death.

B. Donor Fatality

- Collection date,
- What product was collected or attempted to be collected,
- Whether this was a manual or automated collection,

- If automated, the name and model of collection device and device manufacturer,
- Brief description of events that led to the fatality – include an overview of previous donations/health history, approximate frequency of donation, any unusual events that occurred during this or any previous donation, any medical intervention taken or response to the reaction, and time from initiating the blood collection to donor's death.

C. Fatality Associated with Therapeutic Apheresis or Certain Therapeutic Phlebotomies

- Date of therapeutic apheresis (e.g., therapeutic plasma exchange) or therapeutic phlebotomy

NOTE: A report is required for a therapeutic apheresis fatality *only if* blood products (e.g., plasma, albumin), rather than products such as crystalloids or hydroxyethyl starch, were given as part of the procedure. A report is required for a therapeutic phlebotomy fatality *only if* a blood product was collected for manufacturing into transfusable biologicals,

- If product was collected, the product's disposition,
- Whether this was a manual or automated collection (if automated, include manufacturer, name and model of collection device),
- If any blood product(s) was transfused, identify the product and the unit or lot number(s),
- Brief description of events that led to the fatality – include underlying medical condition or disease and circumstances necessitating the therapeutic apheresis or therapeutic phlebotomy, any medical intervention or response to the reaction, and time from initiating the procedure to patient's death.

V. 7-DAY REPORT

You must submit a written report of the fatality investigation to CBER within 7 days after the fatality (21 CFR 606.170(b)). You should identify this report as a follow-up on a fatality notification previously reported to CBER and include the initial notification date. The 7-day report should provide any new findings or information relevant to the fatality that have become available since the initial notification, including your follow-up investigation and conclusions.

The 7-day report should include:

- Discharge summary and/or death certificate,
- Autopsy report (if performed),
- Conclusions and follow-up (frequently referred to in the blood community as a corrective action plan), if appropriate, and
- Either A, B, or C listed below, as appropriate.

We understand that, due to the complexity of some fatality investigations, some of this information may not be available when you submit your 7-day report. In that event, you may amend your 7-day report by filing additional information as it becomes available.

A. Patient/Recipient Fatality

- Complete transfusion reaction report including the results of the clerical, serological, and visual re-checks performed.
- Additional relevant documents including hematology reports; clinical chemistry reports for cardiac and/or liver enzymes, albumin, and bilirubin; viral marker tests; microbiology reports; reports of anti-HLA and/or anti-neutrophil antibody testing; tryptase levels; radiology reports; or physicians' consults/opinions.
- If replacement fluid(s) was given during the transfusion, indicate which fluid(s) and the unit or lot number(s), include any other relevant information, manufacturer's notices, contamination warnings, or replacement fluid recalls.
- If responsibility for the fatality appears to be outside the blood bank, the nurses' and/or physicians' notes on the patient, radiology reports, physicians' consults/opinions.
- Results of lookback investigation, including follow-up testing on implicated donor(s) when the fatality was the result of transfusion transmitted infectious disease such as hepatitis or HIV.
- Meeting minutes or report from your transfusion committee when the fatality was reviewed and discussed. If this incident was reviewed by any other hospital oversight group(s) such as risk management or quality practices, the report or summary of their findings.

B. Donor Fatality

- The deceased's donor record file that includes the donation just before the fatal incident and information on all donations during the past 2 years.
- Lot numbers and expiration dates of collection sets or harnesses; if replacement fluid(s) was given during the collection, indicate which fluid(s) and the unit or lot number(s), include any other relevant information, manufacturer's notices, contamination warnings or replacement fluid recalls.
- Performance log for the device and any other relevant performance logs, maintenance records, manufacturer's notices or recalls on significant machine part(s) on the device/system during the past 2 years.
- If the donor was hospitalized due to the reaction, provide any relevant documents, e.g., reports of laboratory tests, which may help determine the cause of fatality.

C. Fatality Associated with Therapeutic Apheresis or Certain Therapeutic Phlebotomies

- A summary of the deceased's history of previous therapeutic apheresis or therapeutic phlebotomy procedures, including any previous adverse reactions related to the procedures.
- Lot numbers and expiration dates of collection sets or harnesses; if replacement fluid(s) was given at any time during the procedure, indicate which fluid(s) and the unit or lot number(s), include any other relevant information, manufacturer's notices, contamination warnings or replacement fluid recalls.

- A summary of the performance log for the device and any other relevant performance logs, maintenance records, manufacturer's notices or recalls on any significant machine part(s) on the device/system during the past 2 years.
- If the fatality followed therapeutic plasma exchange (TPE) and Fresh Frozen Plasma (FFP) was the replacement fluid, an abbreviated transfusion reaction work up to rule out ABO incompatibility, bacterial contamination, anaphylactic reaction or WBC antibody reaction may be useful.

VI. INQUIRIES

If you have any questions about reporting fatalities, please contact the CBER Fatality Program Manager at 301-827-6220.